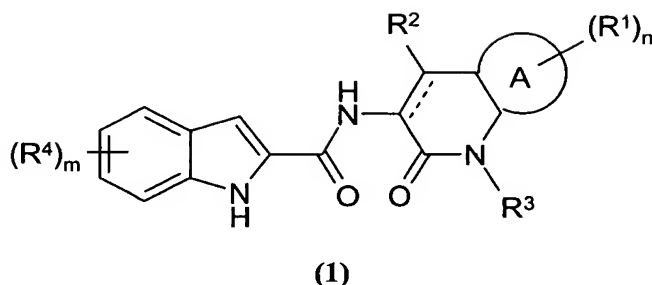


Claims

1. A compound of formula (1):



wherein

----- is a single or double bond;

A is phenylene or heteroarylene;

m is 0, 1, or 2;

n is 0, 1, or 2;

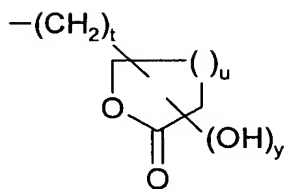
R^1 is independently selected from halo, nitro, cyano, hydroxy, carboxy, carbamoyl, *N*- C_{1-4} alkylcarbamoyl, *N,N*-(C_{1-4} alkyl) $_2$ carbamoyl, sulphamoyl, *N*- C_{1-4} alkylsulphamoyl, *N,N*-(C_{1-4} alkyl) $_2$ sulphamoyl, -S(O) $_b$ C_{1-4} alkyl (wherein b is 0, 1, or 2), C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} alkanoyl, C_{1-4} alkanoyloxy, hydroxy C_{1-4} alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, and trifluoromethoxy; or

when n is 2, the two R^1 groups, together with the carbon atoms of A to which they are attached, may form a 4- to 7-membered ring, optionally containing 1 or 2 heteroatoms independently selected from O, S, and N, and optionally being substituted with one or two methyl groups;

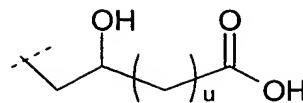
R^4 is independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, and C_{1-4} alkanoyl;

R^2 is hydrogen, hydroxy, or carboxy;

R^3 is selected from hydrogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkanoyl, carbamoyl, C_{3-7} cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, aryl, heterocyclyl, C_{1-4} alkyl (optionally substituted with 1 or 2 R^8 groups), and groups of the formulae B and B'



(B)



(B')

wherein y is 0 or 1, t is 0, 1, 2, or 3 and u is 1 or 2;

provided that the hydroxy group is not a substituent on the ring carbon adjacent to the ring oxygen;

R^8 is independently selected from hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxy, hydroxy C_{1-4} alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, C_{3-7} cycloalkyl, C_{1-4} alkanoyl, C_{1-4} alkoxy, C_{1-4} alkylS(O) $_b$ - (wherein b is 0, 1, or 2), C_{3-6} cycloalkylS(O) $_b$ - (wherein b is 0, 1, or 2), arylS(O) $_b$ - (wherein b is 0, 1, or 2), heterocyclylS(O) $_b$ - (wherein b is 0, 1, or 2), benzylS(O) $_b$ - (wherein b is 0, 1, or 2), -N(OH)CHO, -C(=N-OH)NH $_2$, -C(=N-OH)NHC $_{1-4}$ alkyl, -C(=N-OH)N(C $_{1-4}$ alkyl) $_2$, -C(=N-OH)NHC $_{3-6}$ cycloalkyl, -C(=N-OH)N(C $_{3-6}$ cycloalkyl) $_2$, -COCOOR 9 , -C(O)N(R 9)(R 10), -NHC(O)R 9 , -C(O)NHSO $_2$ (C $_{1-4}$ alkyl), -NHSO $_2$ R 9 , (R 9)(R 10)NSO $_2$ -, -COCH $_2$ OR 11 , (R 9)(R 10)N-, and -COOR 9 ;

R 9 and R 10 are independently selected from hydrogen, hydroxy, C_{1-4} alkyl (optionally substituted with 1 or 2 R 13), C_{3-7} cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C $_{1-4}$)alkyl, trihalo(C $_{1-4}$)alkyl, aryl, heterocyclyl, and heterocyclyl(C $_{1-4}$ alkyl); or

R 9 and R 10 together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring is optionally substituted on carbon with 1 or 2 substituents independently selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, C_{1-4} alkoxy, and heterocyclyl, or the ring may be optionally substituted on two adjacent carbons with -O-CH $_2$ -O- to form a cyclic acetal wherein one or both of the hydrogens of the -O-CH $_2$ -O- group may be replaced by a methyl;

R 13 is selected from hydroxy, halo, trihalomethyl, and C_{1-4} alkoxy; and

R 11 is independently selected from hydrogen, C_{1-4} alkyl, and hydroxy C_{1-4} alkyl; or a pharmaceutically acceptable salt or prodrug thereof.

2. A compound of claim 1, wherein

R^3 is selected from hydrogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkanoyl, carbamoyl, C_{3-7} cycloalkyl (optionally substituted with 1 or 2 hydroxy groups, cyano(C_{1-4})alkyl, phenyl, morpholino, morpholinyl, piperidino, piperidyl, pyridyl, pyranyl, pyrrolyl, imidazolyl, thiazolyl, thienyl, thiadiazolyl, piperazinyl, isothiazolidinyl, 1,3,4-triazolyl, tetrazolyl, pyrrolidinyl, thiomorpholino, pyrrolinyl, homopiperazinyl, 3,5-dioxapiperidinyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrazolyl, pyrazolinyl, isoxazolyl, 4-oxopyridyl, 2-oxopyrrolidyl, 4-oxothiazolidyl, furyl, thienyl, oxazolyl, 1,3,4-oxadiazolyl, and 1,2,4-oxadiazolyl, tetrahydrothiopyranyl, 1-oxotetrahydrothiopyranyl, 1,1-dioxotetrahydrothiopyranyl, and C_{1-4} alkyl (optionally substituted with 1 or 2 R^8 groups);

R^9 and R^{10} are independently selected from hydrogen, hydroxy, C_{1-4} alkyl (optionally substituted with 1 or 2 R^{13} groups), C_{3-7} cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, trihalo C_{1-4} alkyl, aryl, heterocyclyl, and heterocyclyl(C_{1-4} alkyl); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring is optionally substituted on carbon with 1 or 2 substituents selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, and C_{1-4} alkoxy, or the ring may be optionally substituted on two adjacent carbons with $-O-CH_2-O-$ to form a cyclic acetal wherein one or both of the hydrogens of the $-O-CH_2-O-$ group may be replaced by a methyl;

R^8 is independently selected from hydroxy, C_{1-4} alkoxy, C_{1-4} alkoxy, hydroxy C_{1-4} alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, C_{3-7} cycloalkyl, C_{1-4} alkanoyl, C_{1-4} alkoxy, C_{1-4} alkylS(O)_b- (wherein b is 0, 1, or 2), C_{3-6} cycloalkylS(O)_b- (wherein b is 0, 1, or 2), arylS(O)_b- (wherein b is 0, 1, or 2), heterocyclylS(O)_b- (wherein b is 0, 1, or 2), benzylS(O)_b- (wherein b is 0, 1, or 2), $-N(OH)CHO$, $-C(=N-OH)NH_2$, $-C(=N-OH)NHC_{1-4}alkyl$, $-C(=N-OH)N(C_{1-4}alkyl)_2$, $-C(=N-OH)NHC_{3-6}cycloalkyl$, $-C(=N-OH)N(C_{3-6}cycloalkyl)_2$, $-COCOOR^9$, $-C(O)N(R^9)(R^{10})$, $-NHC(O)R^9$, $-C(O)NHSO_2(C_{1-4}alkyl)$, $-NHSO_2R^9$, $(R^9)(R^{10})NSO_2-$, $-COCH_2OR^{11}$, $(R^9)(R^{10})N-$, and $-COOR^9$;

R^{13} is selected from hydroxy, halo, trifluoromethyl, and C_{1-4} alkoxy; and

R^{11} is selected from hydrogen, C_{1-4} alkyl, and hydroxy C_{1-4} alkyl;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

3. A compound of claim 1, wherein:

R^3 is selected from cyano C_{1-4} alkyl and C_{1-4} alkyl (optionally substituted with 1 or 2 R^8 groups);

R^8 is independently selected from hydroxy, phenyl, 2,2-dimethyl-1,3-dioxolan-4-yl[[;]], 2,2-dimethyl-1,3-dioxan-4-yl[[;]], 2,2-dimethyl-1,3-dioxan-5-yl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, pyrrolidinyl, piperidyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl, C_{1-4} alkoxy, C_{1-4} alkanoyl, C_{1-4} alkylS(O)_b- (wherein b is 0, 1, or 2), -C(O)N(R^9)(R^{10}), -COOR⁹, -C(O)NHSO₂Me, -C(=N-OH)NH₂, -C(=N-OH)NHC₁₋₄alkyl, -C(=N-OH)N(C_{1-4} alkyl)₂, and -NHSO₂R⁹; and

R^9 and R^{10} are independently selected from hydrogen, hydroxy, and C_{1-4} alkyl optionally substituted with R^{13} (wherein R^{13} is C_{1-4} alkoxy or hydroxy); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring may be optionally substituted on carbon with 1 or 2 hydroxy groups or carboxy groups), or the ring may be optionally substituted on two adjacent carbons with -O-CH₂-O- to form a cyclic acetal wherein one or both of the hydrogens of the -O-CH₂-O- group may be replaced by a methyl; or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

4. A compound of claim 1, wherein:

R^3 is selected from cyano, C_{1-4} alkyl, and C_{1-4} alkyl (optionally substituted with 1 or 2 R^8 groups);

R^8 is independently selected from hydroxy, 2,2-dimethyl-1,3-dioxolan-4-yl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, tetrazolyl, C_{1-4} alkoxy, C_{1-4} alkanoyl, C_{1-4} alkylS(O)_b- (wherein b is 0, 1, or 2), -C(O)N(R^9)(R^{10}), -COOR⁹, -C(O)NHSO₂Me, and -C(=N-OH)NH₂; and

R^9 and R^{10} are independently selected from hydrogen, hydroxy, and C_{1-4} alkyl optionally substituted with R^{13} (wherein R^{13} is C_{1-4} alkoxy or hydroxy); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring selected from piperidine, 4-hydroxypiperidine, pyrrolidine, 3,4-dihydroxypyrrolidine, and the dimethylacetal of 3,4-dihydroxypyrrolidine; or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

5. A compound of claim 1, wherein:

m is 1 and R⁴ is chlorine;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

6. A compound of claim 1, wherein:

A is phenylene;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

7. A compound of claim 1, wherein:

A is heteroarylene;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

8. A compound of claim 1, wherein:

---- is a single bond;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

9. A compound of claim 1 selected from:

5-chloro-*N*-[1-(methoxycarbonylmethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

N-[1-(carboxymethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-5-chloroindole-2-carboxamide;

5-chloro-*N*-(2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-[{2-oxo-1-[2-oxo-2-(pyridin-2-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylthio)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylsulphonyl)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylsulphonyl)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(1,3,4-thiadiazol-2-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-methylpyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-oxo-1-[2-oxo-2-(pyridin-3-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-methyl-1,3,4-thiadiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-cyano-1*H*-pyrazol-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-methyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-chloropyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-hydroxypyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(pyridin-2-ylmethyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-[2-oxo-2-(pyridin-4-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-methyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(pyrazin-2-ylmethyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-fluoropyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(2-hydroxypyrimidin-4-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-[2-oxo-2-(pyrimidin-4-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-ethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-hydroxypyrimidin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-methylpyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-chloropyridazin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1*H*-imidazol-2-ylmethyl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-methyl-1*H*-pyrazol-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-[2-oxo-2-(2*H*-tetrazol-5-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-ethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-fluoropyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

N-(1-{2-[(6-bromopyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-5-chloro-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(2-hydroxyethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(2,2-dimethyl-1,3-dioxan-5-yl)methyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{3-hydroxy-2-(hydroxymethyl)propyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(2,3-dihydroxypropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(3-hydroxy-2-oxopropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(2*R*)-2,3-dihydroxypropyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(methylsulfonyl)amino]ethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

N-{1-[2-(acetylamino)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-5-chloro-1*H*-indole-2-carboxamide;
5-chloro-*N*-(2-oxo-1-{2-[(trifluoroacetyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;
5-chloro-*N*-[1-(3-hydroxypropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;
N-{1-[(2*Z*)-2-amino-2-(hydroxyimino)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-5-chloro-1*H*-indole-2-carboxamide;
5-chloro-*N*-(6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide; and
5-chloro-*N*-[6-(methyloxy)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;
or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

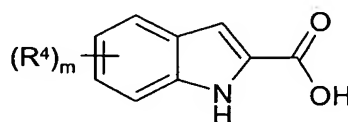
10. A pharmaceutical composition which comprises a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, in association with a pharmaceutically acceptable diluent or carrier.

13. A method for the treatment of type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia, or obesity in a warm-blooded animal, comprising administering a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

14. A method for the treatment of type 2 diabetes in a warm-blooded animal, comprising administering a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

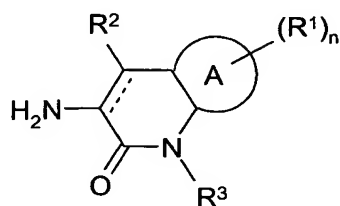
15. A process for the preparation of a compound claim 1, which process comprises:

reacting an acid of the formula (2)



(2)

or an activated derivative thereof; with an amine of formula (3)



(3)

and thereafter if necessary

- i) converting a compound of the formula (1) into another compound of the formula (1);
- ii) removing any protecting groups; or
- iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.